

## Abdominal Pain: A Real Challenge in Novel COVID-19 Infection

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### ABSTRACT

COVID-19 (coronavirus disease 19) is an infectious disease caused by coronavirus 2019-nCoV. Since its detection in China at the end of 2019, the novel coronavirus has rapidly spread throughout the world and has caused an international public health emergency. The most common manifestation is flu-like symptoms. Mild infections usually improve within a few days, but COVID-19 can cause severe pneumonia with acute respiratory distress syndrome and death. Gastrointestinal symptoms are less common but possible and more difficult to recognize as part of a COVID-19 syndrome. In line with the current opinion of the WHO, we strongly believe that preventive measures and early diagnosis of COVID-19 are crucial to interrupt virus spread and avoid local outbreaks. We report the cases of COVID-19 patients admitted to our Emergency Department who complained of gastrointestinal symptoms at admission.

### LEARNING POINTS

- The novel COVID-19 infection is a severe public health problem which is causing an increasing number of deaths worldwide.
- Although uncommon, there may be a relationship between gastrointestinal symptoms and COVID-19, as reported in recent studies.
- Early detection and isolation of patients with COVID-19 infection is the only way to control and limit the global spread of this virus.

### KEYWORDS

COVID-19 infection, abdominal pain, diarrhoea, gastrointestinal symptoms

### INTRODUCTION

The coronaviruses are a large family of viruses that can cause respiratory infections ranging from mild symptoms to severe pneumonia. 2019-nCoV is a new type of coronavirus which was first identified in China. Since its detection in humans at the end of 2019, it has rapidly spread worldwide causing respiratory infections of various degrees of severity. The most common symptoms, which develop within 2–14 days of exposure, are dry cough, fever and fatigue<sup>[1, 2]</sup>. Mild infections may be self-limiting in few days, but in some cases the respiratory symptoms can develop into acute respiratory distress syndrome (ARDS) with a high risk of death from multiorgan failure.

Nasopharyngeal and oropharyngeal swabs can be used to confirm the presence of 2019-nCoV. A CT scan of the chest is the gold standard for diagnosis and assessment of lung involvement. Ground-glass opacity and crazy-craving patterning are the most common radiological signs of COVID-19 pneumonia. CT is commonly used to evaluate lung damage during recovery<sup>[3]</sup>. Recently, we investigated the role of lung US in the early detection of COVID-19 pneumonia and showed a strong correlation between lung US and CT scans in all investigated patients<sup>[4]</sup>. No specific treatment or vaccines against COVID-19 are currently available. COVID-19 patients can be treated with antivirals but there is no clear evidence of benefit<sup>[5]</sup>. The most important way to fight this viral infection is to detect COVID-19 early, isolate cases, trace contacts

and deliver the correct information to the general public<sup>[6]</sup>.

Gastrointestinal involvement, such as abdominal pain, nausea, vomiting and diarrhoea, has been recently reported in the literature<sup>[7]</sup>. Diarrhoea occurs secondary to the interaction between ACE2, highly expressed in the human small intestine, and 2019-nCoV cell entry receptor ACE2. Recent studies show that 2019-nCoV RNA has been detected in stool samples, confirming faecal–oral transmission. According to the literature, the incidence of diarrhoea could be underestimated<sup>[8]</sup>.

In the current case report, we consider COVID-19 infection in the differential diagnosis of gastrointestinal symptoms in 10 patients who referred to our Emergency Department in February 2020, at the beginning of the spread of COVID-19 in Italy.

### CASE DESCRIPTION

Ten patients (6 males, 4 females) with mean age 50±18 years were admitted to our Emergency Department complaining of fever and flu-like symptoms in the previous 5–10 days, with general malaise, decreased appetite, abdominal pain and vomiting/diarrhoea. Only one patient denied cough and fever. None of them had a history of abdominal surgery or a notable medical history, including inflammatory bowel disease. They reported no melena or weight loss. Diarrhoea was defined according the WHO criteria as having three or more loose or liquid stools per day or having more stools than normal. Physical examinations were normal with no distended abdomens, tenderness or hypo/hyperactive bowel sounds. The vital signs were in the normal range with a maximum body temperature of 39°C (37.6±1°C). At admission, four patients complained of dyspnoea with significantly decreased PaO<sub>2</sub>/FiO<sub>2</sub> and a need for oxygen.

A nasopharyngeal swab sample confirmed COVID-19 infection in all patients. The patients' characteristics at admission are reported in Table 1.

	Age (years)	Sex (M, F)	Fever and flu-like symptoms	Dyspnoea	GIT symptoms	Body temperature (°C)	PaO <sub>2</sub> /FiO <sub>2</sub> (mmHg)
Pt 1	44	M	No	No	Diarrhoea	38.7	>300
Pt 2	54	F	Yes	No	Abdominal pain	39.0	>300
Pt 3	39	F	Yes	No	Diarrhoea	36.5	<b>200</b>
Pt 4	44	M	Yes	Yes	Diarrhoea	38.8	>300
Pt 5	56	F	Yes	No	Vomiting	38.5	>300
Pt 6	57	M	Yes	No	Diarrhoea	36.9	<b>275</b>
Pt 7	65	M	Yes	No	Diarrhoea	37.7	>300
Pt 8	22	F	Yes	Yes	Diarrhoea	36.8	<b>261</b>
Pt 9	62	M	Yes	Yes	Vomiting	37.8	<b>271</b>
Pt 10	55	M	Yes	Yes	Vomiting	36.0	<b>200</b>

Table 1. Patients' characteristics at admission

F, female; GIT, gastrointestinal; M, male; Pt, patient. Abnormal values are in red.

Laboratory tests revealed lymphopenia, high C-reactive protein and altered liver enzymes in most of the patients, as reported in Table 2. Tests revealed an average white blood cell count (WBC) of 6.15 (3.2–9.29) ×10<sup>9</sup>/l, platelets (PLT) 176.7 (82–341) ×10<sup>9</sup>/l, and lymphocytes 1.31 (0.60–2.76) ×10<sup>9</sup>/l. The eosinophil percentage was undetectable in all patients. The average value of ALT (alanine aminotransferase) was 77.4 U/l (29–162 U/l), AST (aspartate aminotransferase) was 81.9 (30–284) U/l, and GGT (gamma glutamyltransferase) was 123 (54–218) U/l. Bilirubin was increased in only one patient (pt 2, Table 2) who developed pancytopenia and haemolytic anaemia, which improved with oral steroid therapy. The average value of CRP was 6.6 (1.5–21.37) mg/dl. When measured, procalcitonin was always undetectable, excluding a bacterial infection. Despite the diarrhoea, only two patients had slowly increasing creatinine levels (pt 7 and 9, Table 2). The

serum potassium level was in the normal range in all patients. In the patient who complained only of diarrhoea with no flu-like symptoms (pt 1, Table 1), we performed stool cultures for *Clostridium difficile* and enteric pathogens, which were all negative.

All patients were investigated with bedside US, which showed a diffuse B-pattern, due to a severe loss of aeration, with spared areas with no pleural effusion; in six patients subpleural consolidation in the lower lobes was detected. Chest CT confirmed COVID-19 pneumonia with typical imaging signs of ground-glass opacity, patchy consolidation and crazy-paving patterning, which were also detected by lung US. An X-ray of the abdomen was performed in only one patient (pt 2, Table 1) and was normal. US of the abdomen did not reveal an abnormal stomach and bowel distention, except in one female patient (pt 8, Table 1) who had bowel inflammatory signs (peri-intestinal inflammatory reaction) as confirmed by a CT scan of the abdomen. This patient completely recovered after antiviral treatment and was discharged home with no signs of bowel disease on US of the abdomen.

All the patients were treated with supportive care and antiviral therapy, including lopinavir and ritonavir tablets. Diarrhoea completely resolved. Six patients have been discharged with the diagnosis of 'COVID-19 pneumonia and diarrhoea'. Four patients (pt 3, 7, 9, 10, Tables 1 and 2) developed acute severe respiratory distress syndrome requiring immediate intubation. They are still in Intensive Care Unit at the time of writing.

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6	Pt 7	Pt 8	Pt 9	Pt 10
WBC ( $10^9/l$ )	9.20	3.40	4.03	4.91	6.24	9.85	5.40	3.20	6.04	9.29
Neutrophil count ( $10^9/l$ )	5.73	1.40	3.21	3.28	3.68	8.61	3.54	2.39	4.46	7.43
Lymphocyte count ( $10^9/l$ )	2.76	1.69	0.60	1.08	1.99	0.94	1.32	0.66	0.86	1.20
Eosinophil count ( $10^9/l$ )	0	0	0	0	0	0	0	0	0	0
PLT count ( $10^9/l$ )	148	82	162	168	143	262	150	165	146	341
CRP (<0.5 mg/dl)	5.3	1.54	6.15	1.5	1.19	6.53	2.55	4.09	21.37	15.85
PCT (>0.5 ng/ml)	ND	0.03	ND	ND	ND	ND	0.36	0.02	ND	0.32
AST (10–37 U/l)	111	35	82	29	45	162	47	95	86	82
ALT (10–37 U/l)	101	53	60	30	46	284	57	67	68	53
GGT (7–40 U/l)	138	99	133	ND	ND	54	96	175	71	218
Total bilirubin (0.1–1.1 mg/dl)	0.84	1.33	0.63	0.53	0.47	0.79	0.60	0.58	0.71	0.95
LDH (0–248 U/l)	400	223	634	251	254	343	244	453	594	964
Lipase (7–60 U/l)	133	22	61	42	42	22	24	169	26	175
Creatinine (0.6–1.2 mg/dl)	1.10	0.41	0.68	1.04	0.59	0.94	1.20	0.72	1.25	1.18
Blood urea nitrogen (10–50 mg/dl)	33	19	28	ND	ND	ND	36	21	42	43
Potassium (3.5–5.0 mEq/l)	4.3	4.0	3.8	3.5	3.7	3.7	4.3	3.8	4.4	4.4

Table 2. Laboratory findings at admission

ALT, alanine transaminase; AST, aspartate transaminase; CRP, C-reactive protein; GGT, gamma glutamyltransferase; ND, not done; PCT, procalcitonin; PLT, platelet; WBC, white blood cell count. Normal range values are in brackets. Abnormal values are in red

## DISCUSSION

Abdominal pain is a real challenge for critical care physicians since there are many potential diagnoses. Signs and symptoms are often non-specific and can mask life-threatening conditions. The consequences of wrongly attributing the pain can be serious for patients. Although gastrointestinal symptoms are less common in patients with COVID-19 infection, the diagnosis of coronavirus disease 2019 cannot be excluded and must be investigated in all patients referred to the Emergency Department. We strongly recommend bedside lung US to detect signs of interstitial pneumonia even in absence of respiratory symptoms. Early suspicion and diagnosis are essential to contain the global spread of COVID-19 infection and its potentially fatal complications, such as acute respiratory distress syndrome.

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